REMARKS

The Office Action mailed March 23, 2005, has been received and carefully reviewed. Claims 20 and 35 having been amended, the pending claims are claims 1-38. Reconsideration and withdrawal of the rejections is respectfully requested.

Claim 20 has been amended to recite a "pulsed" extraction field and that the ion bunch travels "for a predetermined time whereby the ions with different mass-to-charge ratios travel different distances." Claim 35 has likewise been amended to recite a "pulsed" extraction field and the additional step of "allowing said ions to travel for a predetermined time in a field free region whereby the ions with different mass-to-charge ratios travel different distances" prior to laterally accelerating the ion stream. Support for the amendment is found, for example, in claim 14 as originally filed. The amendment is made to clarify the invention.

Information Disclosure Statement mailed November 24, 2004

Applicants note that an Information Disclosure Statement was mailed on November 24, 2004, transmitting a From 1449 listing 12 United States patents and 2 other documents (**Exhibit A**). Copies of the two other documents were included with the submission. This 26 page submission is evidenced by the Auto-Reply Facsimile Transmission (**Exhibit B**). It is respectfully requested that the documents cited in the Information Disclosure Statement mailed November 24, 2004, be considered by the Examiner and that the initialed and signed Form 1449 be returned with the next Official Communication. If the Office has misplaced the two cited non-patent documents, please feel free to contact the undersigned directly for replacement copies to facilitate prosecution.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 38 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleges that there is insufficient

antecedent basis for the phrase "provide one mass unit for other specific mass-to-charge ratio resolution by determining separation distances between the separate detectors derived from a relation of position along the flight path with respect to adjacent unit mass to charge ratio values within the range." This rejection is respectfully traversed.

Claim 38 depends from claim 36 and, as such, ultimately from claim 35. Claim 38 recites the step of "arranging" the "separate ion detectors." "Separate detectors" that detect "ion intensity" have antecedent basis, for example, in claim 35. Claim 35 further recites that the "separate detectors" are "spaced from the acceleration region each by respective distances that differ from each other." Thus the relative positioning between the separate detectors also has antecedent basis in claim 35, and the resulting space between the separate detectors is readily understood as a separation distance.

Claim 38 recites arranging the separate ion detectors so as "to provide one mass unit for other specific mass-to-charge ratio resolution." The arrangement which provides this level of resolution is identified "by determining separation distances between the separate detectors derived from a relation of position along the flight path with respect to adjacent unit mass to charge ratio values within the range." As noted in the paragraph 30 of the specification there "is a separate detector for each ion mass resolution element." Further, as noted in paragraph 72 of the specification, the spacing between the detectors is related to resolution of different m/z species. For example, in the instrument described at paragraph 72, "[d]etectors separated by 40 microns will provide unit m/z resolution."

It is respectfully submitted that claim 38 finds clear support and/or antecedent basis in the description as required by 37 C.F.R. 1.75 and MPEP 608.01(g).

Rejection under 35 U.S.C. §102

The Examiner rejected claims 1-12, 14-19, and 35-37 under 35 U.S.C. §102(b) as being anticipated by Bateman et al (U.S. Patent No. 2001/0052569; "Bateman"). This rejection is respectfully traversed.

Claim 1 reads as follows:

1. A mass analyzer including:
a. an ion storage device for receiving and storing ions;
b. a means for applying an ion extraction voltage pulse to said storage device to accelerate the ions whereby ions leaving the storage means have mass-to-charge ratio dependent velocities;
c. a field free region through which the ions of different mass-to-charge ratios travel different distances in a predetermined time, and
d. detectors spaced to receive the ions of different mass-to-charge ratios which have traveled different distances in a predetermined time and provide outputs indicative of the mass-to-charge ratio of the received ions.

To anticipate a claim, a reference much teach each and every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631; 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

It is respectfully submitted that Bateman does not teach each and every element of claims 1-12, 14-19, and 35-37.. For example, contrary to the statements of the Examiner and as described in more detail below, Bateman does not teach ion storage (e.g., independent claims 1, 14, 15, 16 and 35), an ion extraction voltage pulse (e.g., independent claim 1), a field free region (e.g., independent claims 1, 14, 16 and 35) through which the ions of different mass-to-charge ratios travel different distances in a predetermined time (e.g., claims 1, 14 and 16), or multiple detectors spaced differently (e.g., independent claims 1, 14, 16 and 35) to receive the ions of different mass-to-charge ratios which have traveled different distances in a predetermined time (e.g., claims 1, 16). Note further that the Examiner has acknowledged at paragraph 12 of the Office Action, in connection with the rejection under 35 U.S.C. §103 discussed below, that Bateman fails to teach the feature of having a plurality of separate detectors spaced from the acceleration region. Since the independent claims are not anticipated by Bateman, dependent claims 2-12,18, 19, 36 and 37 are not anticipated by Batemen at al. for at least the same reasons.

Brief description of the invention

The mass analyzer of the present invention includes a means for applying an ion extraction voltage pulse to accelerate ions from an ion storage device along a horizontal axis, as shown in Fig. 1 (see, for example, paragraph 0032 of the specification). For convenience, this horizontal dimension will be termed the "axial" direction, to distinguish it from optional subsequent off-axis, transverse, lateral or orthogonal ion acceleration. The axial direction defines the direction of the ion beam along the main ion path. In the present invention, it is the direction the ions are moving after exiting from the ion storage device.

The accelerated ions have velocities in the axial direction that depend on their mass-to-charge ratios. Accelerated ions with different mass-to-charge ratios travel different distances in a predetermined time. Because they are accelerated with an extraction pulse and not through continuous extraction, by the time they reach the orthogonal field extraction region the ions are dispersed in the axial direction according to their m/z values (see, for example, paragraph 0033 of the specification). The accelerated ions are thus mass discriminated in space along the main ion stream flight path (i.e., in the axial direction) during the predetermined time due to their different velocities. See Fig. 1, where ions having different m/z values are denoted by different sizes of circles. Ions of different mass-to-charge ratios which have traveled different distances in the predetermined time are detected with the detectors of the mass analyzer. Because the ions are separated in space on the basis of their m/z values, each detector detects ions with a different range of m/z values.

Notably, the present invention utilizes *pulsed* ion extraction, not continuous ion extraction. Pulsed extraction produces mass discrimination along the main ion stream flight path in the axial direction. This is how the ions with different mass-to-charge ratios are separated in space, since they travel different distances in the axial direction in a predetermined time. This is the "distance-of-flight" component of the present device and methods.

Response to rejection under 35 U.S.C. §102

Bateman teaches a device comprising an ion source 1, a optional ion guide 2, a mass filter 3, a collision cell 4, and an orthogonal acceleration time-of-flight mass spectrometer 5. Within the time-of-flight mass spectrometer 5 are three additional components along the transverse axis as shown in Bateman Fig. 1, represented by three rectangles. For purposes of discussion, let us number them "7," "8" and "9" from left to right, in which case component "7" serves as an orthogonal deflector and component "9" serves as a detector (no function is specified for "8").

The claimed device and method differs from the device and method described in Bateman in numerous respects, and is patentably distinct therefrom. Further, it is respectfully submitted that the Bateman device has been inadvertently mischaracterized by the Examiner in a number of different ways, only some of which will be pointed out herein for sake of brevity. For example, contrary to the contention of the Examiner, Bateman does not teach an ion storage device, storage of ions prior to acceleration, trapping of ions, an ion storage means, an ion store, or the like (e.g., claims 1, 14-16, 20 and 35). Component 1 is an ion source, and components 2 (optional ion guide), 3 (mass filter) and 4 (collision cell) are all transmission devices, not ion storage devices. There is no counterpart in Bateman to the "ion storage device" included in the mass analyzer of the present invention. Thus, the Examiner errs in stating that Bateman teaches an "ion storage device" or "trapping of ions in an ion storage device."

Nor does Bateman teach an ion extraction voltage "pulse" applied to an ion storage device or stored ions (e.g., claims 1, 20 and 35, as amended). At paragraph 0088, Bateman describes the continuous transmission of ions through the various components of the device, and states that other optical components may be present to "maximise ion transmission between various parts of the apparatus."

Bateman also does not teach a "field free region" through which the ions of different mass-to-charge ratios travel different distances in a predetermined time (e.g., claims 1, 14, 16, 20 and 35). To the contrary, the region between collision cell 2 through the orthogonal deflector "7" (first of three boxes in orthogonal time of flight mass analyzer 5) in Bateman Fig. 1 is not

field free because an axial field must be imposed on the ions subsequent to fragmentation in order to move them axially.

Bateman also does not teach detectors "spaced to receive the ions of different mass-to-charge ratios which have traveled different distances in a predetermined time" (e.g., claims 1, 15 and 16). Indeed, Bateman does not teach more than one detector at all. The ion stream in the axial direction in the Bateman device is continuous, therefore each segment of this stream contains ions of all m/z values proceeding from the ion source. Multiple detectors, if present, could not discriminate ions having different charge-to-mass ratios.

With respect to claims 1-12, at paragraph 5 of the Office Action mailed March 23, 2005, the Examiner asserts that Bateman teaches a "transverse deflection field to the ion stream after the formation of product ions so that precursor and product ions are separated transversely according to their mass-to-charge ratios," either before or after the orthogonal acceleration region. Applicant is confused by the Examiner's use of the word "transverse"–does this mean in the axial direction, or does it mean lateral or orthogonal thereto (i.e., off-axis)? Clarification concerning the meaning of the term and its relation to the invention as claimed is requested if the Examiner continues to assert the objection. In any event, however, as noted above, each point along the axial ion stream in the Bateman device contains ions of all m/z values, including that segment within deflector 7 that is subject to the orthogonal acceleration. Separation of ions according to their mass-to-charge ratios in the axial direction in the Bateman device cannot happen without a time variant extraction pulse to produce the stream of ions in the axial direction. In the Bateman device, ion extraction is continuous, not pulsed, and therefore the Bateman device does not discriminate ions on the basis of m/z values in the axial direction.

Pulsing does occur in the Bateman device, but is orthogonal to the ion stream. It is used for the purpose of determination of ion m/z through the well known method of orthogonal time-of-flight mass spectrometry in which an ion's m/z is determined by the time between the applied orthogonal pulse and its arrival at the detector. The particular detector at which an ion arrives is not used (nor could it be used) as an indication of ion m/z because the ions have not been bunched or pulse-extracted in the horizontal (axial) direction, and ions of differing m/z therefore

have no distinct lateral position within the ion stream passing through the orthogonal acceleration region. Thus, contrary to the assertion of the Examiner in paragraph 5, Bateman does not teach a "detectors positioned to enable position dependent detection" since the content of the ion stream at any position prior to the orthogonal pulse is not position dependent.

In the present invention, the first time variant pulse takes the form of pulsed ion extraction in the axial direction, providing m/z discrimination on the basis of distance of flight. The orthogonal or lateral acceleration that optionally follows (e.g., claim 5) provides a second dimension for m/z analysis, based on time of flight to the detectors. Importantly, each detector in the claimed device detects ions with different m/z values from the other detectors. In Bateman, if multiple detectors were to be used (and Bateman does not teach multiple detectors) the same information would be detected by each detector.

Bateman also does not teach a "means for dissociating or changing the mass-to-charge ratio of [extracted] ions in said field free region into product ions so that said product ions travel at substantially the same velocity as their precursor ions" (Office Action at paragraph 5) prior to orthogonal acceleration (e.g., claim 6). The Examiner cites paragraph 0018-0022 of Bateman for this alleged teaching. There is nothing in the cited passage, or anywhere else in the Bateman document, to teach or suggest that product ions travel at substantially the same velocity as their precursor ions. To the contrary, in the Bateman device fragmentation occurs as a result of collisions in the collision cell under conditions that slow the ions down so that they exit from the collision cell at a nearly uniform ion energy, independent of mass, not a constant speed or velocity, and not a velocity that is related to the precursor m/z. All the ions (precursors and products) therefore have essentially the same mass dependent velocities after fragmentation. Therefore Bateman does not teach that fragmentation occurs in such a way that precursors and fragments thereof (products) have the same velocity after dissociation.

To reiterate, because ion extraction in the Bateman device is continuous, the ions are not separated by mass at all in the transverse direction within the ion stream. Bateman does not teach or suggest discriminating ions by mass using "distance of flight"; there simply cannot be

any mass discrimination that is based on "distance-of-flight" when all ions are present at all distances. Continuous extraction causes ions of all mass-to-charge ratios (i.e., both precursor and daughter ions, as defined by the quadrupole mass filter 3) to be present at all points (distances) along the ion stream flight path axis, including that portion of the ion stream that is orthogonally accelerated in the orthogonal acceleration region of the device. The detector "7" in Bateman permits mass discrimination using orthogonal time of flight analyzer 5 according to conventional time-of-flight methodology only, not based on distance traveled by any of the ions. With respect to claim 1 and those dependent therefrom, the Bateman device does not include, for example, an "ion storage device for receiving and storing ions" or a "means for applying an ion extraction voltage pulse to said storage device to accelerate the ions." It therefore cannot mass discriminate ions on the basis of the distance traveled. Because the ions that are subjected to the orthogonal pulse in Bateman are not ions that have been mass discriminated along the ion stream axis, the Bateman device also does not include, for example, "detectors spaced to receive the ions of different mass-to-charge ratios which have traveled different distances in a predetermined time" (e.g., claim 1). Indeed, Bateman does not teach or suggest multiple detectors at all. The device of claim 1 is accordingly not anticipated by Batemen, since Bateman does not describe each component of the claimed device. Likewise, for at least these reasons, dependent claims 2-12 are not anticipated by Bateman.

The methods of claims 14-17 are also not anticipated by Bateman, for reasons set forth above. For example, Bateman does not describe "trapping ions in an ion storage device" or "allowing [the extracted] ions to travel for a predetermined time in a field free region whereby they travel different distances; and detecting the ions of different mass-to-charge ratio with detectors which are spaced substantially parallel to the line of travel" (claim 14), or "determining the mass-to-charge ratios of said ions by the distance traveled by ions of different mass-to-charge ratio in a predetermined time" (claim 15), or "detecting said ions with ion detectors spaced to receive ions of different mass-to-charge ratio which have traveled different distances in a predetermined time" (claim 16). Moreover, contrary to the statement of the Examiner at paragraph 8, Bateman does not teach "periodically" applying an extraction voltage (claim 16).

Since in Bateman, there is no periodically applied extraction voltage, there is no flight time reference with which the ions can be detected at a single flight time that applies to all ions in the ion stream.

Claim 35-37 are likewise not anticipated by Bateman. Claim 35, as amended, recites a "accelerating ions from an ion store by applying a pulsed extraction field" and "allowing [the extracted] ions to travel for a predetermined time in a field free region whereby the ions with different mass-to-charge ratios travel different distances," followed by "laterally accelerating the ion stream within the field free region to reach adjacent ones of separate detectors in a detector array, the separate detectors being spaced from the acceleration region each by respective distances that differ from each other." These features, as well as others, are not described in Bateman since Bateman does not describe mass discrimination using distance of flight.

For at least these reasons, it is respectfully submitted that claims 1-12, 14-19, and 35-37 are not anticipated under 35 U.S.C. §102(b) by Bateman.

Rejection under 35 U.S.C. §103

The Examiner rejected claims 13 and 20-34 under 35 U.S.C. §103 as being unpatentable over Bateman et al (U.S. Patent No. 2001/0052569) in view of Schwartz et al (U.S. Patent No. 6,797,950). This rejection is respectfully traversed.

Claim 20, as amended, is drawn to a mass spectrometer that includes, *inter alia*, a pulsed extractor field to extract and accelerate a bunch of ions from the ion storage device to accelerate ions of smaller mass-to-charge ratio at a greater velocity than ones of larger charge-to-mass ratio, a field free region through which the ion bunch travels for a predetermined time whereby the ions with different mass-to-charge ratios travel different distances, and a plurality of separate detectors spaced from the acceleration region each by respective distances that differ from each other.

As noted above, Bateman does not teach or suggest, for example, an ion storage device or separation of ions in the ions stream flight path on the basis of mass-to-charge ratio, e.g., by way of pulsed extraction. Nor does Bateman teach multiple detectors. It is respectfully submitted

that the Examiner is incorrect in stating that Bateman teaches, *inter alia*, a mass spectrometer "wherein the detectors are arranged parallel to the line of travel (figure 1); [and] wherein the detectors present the ion intensities in reverse order of distance of the detectors from the extraction region to produce a mass spectrum (figure 1)". To the contrary, Figure 1 of Bateman shows only one detector, component 9. Should the Examiner disagree, Applicant requests that the Examiner specifically identify the multiple detectors in the Bateman device.

Schwartz does not remedy the deficiency in Bateman because neither Schwartz nor Bateman teach a plurality of separate detectors spaced from the acceleration region each by respective distances that differ from each other, the separate detectors being configured and arranged to detect ion intensity of the smaller and larger mass-to-charge ratio ions that reach them (claim 20).

Moreover, as noted above, the ion stream in the axial direction in the Bateman device is continuous, therefore each segment of this stream contains ions of all m/z values proceeding from the ion source. Multiple detectors, if present, could not discriminate ions having different charge-to-mass ratios. There is no motivation in either Bateman or Schwartz to modify the Bateman device to include separate detectors spaced from the acceleration region each by respective distances that differ from each other, since each detector would report the same information. It further follows that application of a lateral acceleration in the device of claim 20 to cause the ions to change their direction of travel laterally to reach adjacent ones of the separate detectors would not result in detection of ion intensity of the smaller and larger mass-to-charge ratio ions that reach them, no matter how the detectors were arranged. The combination of Bateman and Schwartz would yield an inoperative invention.

Similar arguments are applicable to the rejection of claim 13 under 35 U.S.C. §103, although no explicit reasons for the rejection claim 13 were given by the Examiner. Moreover, claim 13 depends from claims 1, which Applicant alleges is patentable over the cited art for reasons described above in connection with the rejection under 35 U.S.C. §102.

For at least these reasons, it is respectfully submitted that claims 13 and 20-34 are not obvious over Bateman in view of Schwartz et al.

Summary

It is respectfully submitted that the pending claims 1-38 are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to contact Applicant's Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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By
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail **Stop Amendment**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 19th day of August, 2005, at 1:30pm (Central Time).

By: [signature]
Name: JACQUELYN K. TORBORG

OMB No. 0651-0011
Page 1 of 1

INFORMATION DISCLOSURE STATEMENT	Atty. Docket No.: 310.002300101	Serial No.: 10/804,968
	Applicant(s): Christie G. Enke	Confirmation No.: 7863
	Application Filing Date: March 18, 2004	Group: 2881
	Information Disclosure Statement submitted via facsimile on: 11-24-04	

EXHIBIT A

U.S. PATENT DOCUMENTS

Examiner Initial	Copy Enclosed	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
		3,953,732	04/27/1976	Oron et al.			
		5,206,508	04/27/1993	Alderdice et al.			
		5,233,189	08/03/1993	Wollnik			
		5,420,423	05/30/1995	Linden			
		5,801,380	09/01/1998	Sinha			
		5,825,025	10/20/1998	Kerley			
		5,872,356	02/16/1999	Fischer et al.			
		6,107,623	08/22/2000	Bateman et al.			
		6,204,500	03/20/2001	Whitehouse et al.			
		6,483,109	11/19/2002	Reinhold et al.			
		6,489,610	12/03/2002	Barofsky et al.			
		6,507,019	01/14/2003	Chernushevich et al.			

FOREIGN PATENT DOCUMENTS

Examiner Initial	Copy Enclosed	Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
		NONE						

OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)

Examiner Initial	Copy Enclosed	Document Description
	X	Enke, "Simultaneous MS/MS, All The Products Of All The Precursors All The Time," PowerPoint Poster presented at American Society of Mass Spectroscopy, June 2003, Montreal, Quebec, Canada (21 pages).
	X	Enke, "Slide 12: A Complete MS/MS Every Pulse," PowerPoint Poster presented at Purdue University on September 20, 2002 (1 page).

EXAMINER	Date Considered

*Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

USPTO 11/24/2004 2:05 PM PAGE 1/001 Fax Server
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EXHIBIT B

TO: Fax Sender at 6123051228

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11-24-2004 12:51 FAX 6123051228 MUETING RAASCH GEBHARDT 001

PATENT
Docket No. 310.00230101

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Christie G. Enke
Serial No.: 10/804,968
Confirmation No.: 7803
Filed: March 18, 2004
For: DISTANCE OF FLIGHT SPECTROMETER FOR MS AND SIMULTANEOUS SCANLESS MS/MS

Group Art Unit: 2881
Examiner: Unassigned

FACSIMILE TRANSMISSION TO THE PTO

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FAX NUMBER: (703) 872-9306
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X Information Disclosure Statement (2 pgs); 1449 form (1 pg); and two documents (22 pgs total) cited on the 1449 form.

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Mueting, Raasch & Gebhardt, P.A.
Customer Number: 26813

Nov. 24, 2004
Date

By: Victoria A. Sandberg
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November 24, 2004
Date

Signature: [signature]
Name: Tam Hoa

If you do not receive all pages, please contact us at (612)305-1220 (ph) or (612)305-1228 (fax).

PAGE 1/26 * RCVD AT 11/24/2004 1:53:19 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/19 * DNIS:2738300 * CSID:6123051228 * DURATION (mm-ss):05-01